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REVIEW ON THYROID DISORDERS

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Abstract

The thyroid hormones control the metabolism of cells, which is their speed of activity. Thyroid hormones regulate the rate of oxygen consumption. Although Thyroid hormones have a similar effect and influence the proper working of all body cells, their action is particularly evident in certain tissues and for certain functions. The relationship between breast cancer and thyroid diseases is controversial. The incidences of autoimmune and non autoimmune thyroid diseases were investigated in patients with breast cancer and age-matched control individuals without breast or thyroid disease. This review focuses on follicular-patterned lesions of the thyroid gland and their differential diagnosis. Included are a discussion of the features differentiating follicular adenoma from adenomatous or hyperplastic nodule and follicular adenoma from follicular carcinoma and the follicular variant of papillary thyroid carcinoma.

INTRODUCTION

The thyroid is able to compensate, continue to produce a normal amount of thyroid hormone despite disruption, in response to some of these agents by increasing serum TSH. The success of this compensation can be assessed in the adult based on markers of thyroid hormone action, but is much more difficult to determine during fetal development and in infants and children. Brain development is the best characterized pathway that is thyroid hormone dependent and vulnerable to thyroid hormone disruption .Local thyroid hormone activation and timing of availability of tri- iodothyronine (T3) is critical in brain and sensory development Agents that interfere with thyroid hormone signalling during this period are the most difficult to detect and quantitate. A significant focus in clinical thyroid disease is to detect and evaluate thyroid disease at the earliest stages .Recent efforts in assessing the impact of environmental agents that disrupt thyroid function have focused on identifying the earliest and subtle effects [1].The sensitive thyroid stimulating hormone (TSH or thyrotropin) assay has become the single best screening test for hyperthyroidism and hypothyroidism, and in most outpatient clinical situations, the serum TSH is the most sensitive test for detecting mild thyroid hormone excess or deficiency. Therapeutic options for patients with Graves' disease include thyroidectomy (rarely used now in the United States), anti thyroid drugs (frequently associated with relapses), and radioactive iodine (currently the treatment of choice). In clinical hypothyroidism, the standard treatment is levothyroxine replacement, which must be tailored to the individual patient. Awareness of subclinical thyroid disease, which often remains undiagnosed, is emphasized, as is a system of care that incorporates regular follow-up surveillance by one physician as well as education and involvement of the patient [2].

HISTORY

Problems with the thyroid gland are extremely common. It has been estimated that as many as one and a half billion people in the world are at risk for thyroid problems. Hypothyroidis the most common thyroid malfuntion but it is possible to have a hyperactive thyroidgland[3.]

Subclinical hypothyroidism is also an important condition, affecting up to 20% of persons beyond 60 years of age. Clinical endocrinologists agree that most patients with subclinical hypothyroidism require therapy [3]. Although patients with this disorder can be asymptomatic, Some patients have subtle findings, including alterations in lipid metabolism, cardiac, gastrointestinal, neuropsychiatric, and reproductive abnormalities, and an increased likelihood of developing a goiter. For increased recognition of subclinical hypothyroidism, physician education and patient awareness are necessary [4].

SYMPTOMS

HYPERTHYROIDISM

The following list illustrates the spectrum of possible signs and symptoms associated with the various causes of hyperthyroidism [5]:

• Nervousness and irritability

• Palpitations and tachycardia

• Heat intolerance or increased sweating

• Tremor

• Weight loss or gain

• Alterations in appetite

• Frequent bowel movements or diarrhoea

• Dependent lower-extremity edema

• Sudden paralysis

• Exertional intolerance and dyspnea

• Menstrual disturbance (decreased flow)

• Impaired fertility

• Mental disturbances

• Sleep disturbances (including insomnia)

• Changes in vision, photophobia, eye irritation, diplopia, or exophthalmos

• Fatigue and muscle weakness

• Thyroid enlargement (depending on cause)

• Pretibial myxedema (in patients with Graves' disease)

A patient with hyperthyroidism need not have all these symptoms.

HYPOTHYROIDISM

The symptoms are generally related to the duration and severity of hypothyroidism, the apidity with which hypothyroidism

occurs, and the psychologic characteristics of the patient. The signs and symptoms of hypothyroidism can include one or more of the following [6]:

• Fatigue

• Weight gain from fluid retention

• Dry skin and cold intolerance

• Yellow skin

• Coarseness or loss of hair

• Hoarseness

• Goiter

• Reflex delay, relaxation phase

• Ataxia

• Constipation

• Memory and mental impairment

• Decreased concentration

• Depression

• Irregular or heavy menses and infertility

• Myalgias

• Hyperlipidemia

• Bradycardia and hypothermia

• Myxedema fluid infiltration of tissues

Although most physicians can diagnose and treat hypothyroidism, in certain situations a clinical endocrinologist experienced in the spectrum of thyroid disease would be most likely to recognize the more subtle manifestations of hypothyroidism and most skilled in the physical examination of the thyroid gland. Consultation with an endocrinologist is recommended in the following situations:

• Patients of age 18 years or less

• Patients unresponsive to therapy

• Pregnant patients

• Cardiac patients

• Presence of goiter, nodule, or other structural changes in the thyroid gland

• Presence of other endocrine disease

Not all patients with chronic thyroiditis have hypothyroidism, and if it is present, it may not persist. Rarely Patients with chronic thyroiditis have a change from a hypothyroid to an onsuppressible euthyroid state or even to a hyperthyroid state because of the development of

Stimulating TSH receptor auto antibodies (TSI or TRAb) of Graves' disease.

CAUSES OF HY PERTHYROIDISM

Hyperthyroidism is the consequence of excessive thyroid hormone action. The causes of hyperthyroidism include the following [7]:

• Toxic diffuse goiter (Graves' disease)

• Toxic adenoma

• Toxic multinodular goiter (Plummer's disease)

• Painful subacute thyroiditis

• Silent thyroiditis, including lymphocytic and post partum variations

• Iodine-induced hyperthyroidism (for example, related to amiodarone therapy)

• Excessive pituitary TSH or trophoblastic disease

• Excessive ingestion of thyroid hormone.

CAUSES OF HYPOTHYROIDISM

Hypothyroidism results from under secretion of thyroid hormone from the thyroid gland. In the United States, the most common cause of primary hypothyroidism is chronic autoimmune thyroiditis (Hashimoto's disease). Other causes are surgical removal of the thyroid gland, thyroid gland ablation with radioactive iodine, external irradiation, a radio synthetic defect in iodine organification, replacement of the thyroid gland by tumor (lymphoma), and drugs such as lithium or interferon. Secondary causes of hypothyroidism include pituitary and hypothalamic disease. Patients should undergo assessment for the cause of their hypothyroidism [8].

PATHOLOGY OF THYROD DISORDER

THYROID GLAND

The thyroid gland consists of a pair of lobes (left and right), each about the size of a small hen's egg, that are located just behind the larynx in the horse's throatlatch area. The thyroid gland produces two principal hormones: thyroxine (T4) and tri-iodothyronine (T3). These hormones have wide-ranging effects on the body, but their most fundamental role in the adult body is to stimulate metabolism. The secretion of these hormones by the thyroid gland is regulated by the pituitary gland (a small gland at the base of the brain). Among

several other regulatory hormones, the pituitary gland secretes a hormone called thyrotropin or thyroid stimulating hormone (TSH). As its name indicates, TSH stimulates the thyroid gland to secrete T4 and T3. But that's not all; secretion of TSH by the pituitary gland is regulated by the hypothalamus (a discrete area of the brain, located just above the pituitary gland). The hypothalamus secretes thyrotropin releasing hormone (TRH) which directs the pituitary gland to secrete TSH. Blood levels of T4 and T3 are kept within a fairly narrow range through a refined feedback loop involving all three of these tissues (thyroid gland, pituitary gland, and hypothalamus). A drop in T4/T3 stimulates TRH production, which stimulates TSH production, which then stimulates the thyroid gland to secrete more T4 and T3. Elevations in T4/T3 have the opposite effect: they suppress the release of TRH and TSH, and thus of T4 and T3 [9].
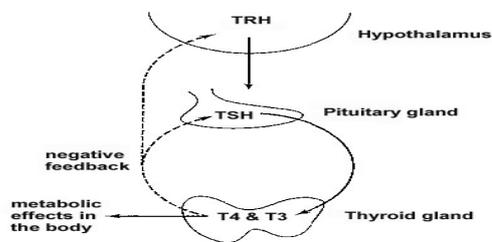
THROID CANCER

The term follicular in thyroid specimens is used by pathologists to designate cell of origin, ie, lesions of follicular cell origin (capable of producing thyroid hormone and thymoglobulin) and to describe the architecture or growth pattern, ie, follicular patterned. According to the classic pathologic description, follicular adenoma is a solitary lesion in an otherwise normal gland; it is completely encapsulated and lacks any capsular and/or vascular Invasion into the tumour capsule and surrounding thyroid. Follicular adenomas usually show either a micro follicular or a macro follicular growth pattern and are devoid of degenerative changes (lesions that have not undergone fine-needle aspiration [FNA] as mentioned for hyper plastic nodules [10].

MALIGNANT FOLLICULAR-PATTERNED LESIONS FOLLICULAR CARCINOMA

This follicular-derived malignant tumour of the thyroid is characterized by follicle formation and lacks nuclear features of papillary thyroid carcinoma (PTC). Two types have been described: the

encapsulated and the widely invasive variant [11].

BENIGN FOLLICULAR-PATTERNED LESIONS

Hyperplastic Nodule and Follicular Adenoma Follicular-patterned hyperplastic nodules usually arise in a background of nodular goiter, can show complete or partial encapsulation, and usually contain a mixture of macrofollicles and microfollicles changes such as hemorrhage, fibrosis, and cyst formation [12].

FOLLICULAR VARIANT OF MEDULLARY CARCINOMA: MIXEDTUMORS

These rare tumors are mentioned in this review for completeness. The presence of follicular or glandular structures in a medullary carcinoma can result from a true follicular pattern of growth or entrapment of neighbouring follicles by invasive tumor. True follicular differentiation of C-cell tumors can occur. These are calcitonin-producing lesions [13].

ROLE OF AUTOIMMUNE THYROID DISEASE IN BREAST CANCER

Breast cancer is a hormone-dependent neoplasm. Many studies showed that thyroid diseases are common among women with breast cancer .whereas other reports did not confirm such an association of breast cancer with thyroid diseases. Almost every form of thyroid disease, including nodular hyperplasia hyperthyroidism and thyroid cancer has been identified in association with breast cancer. These findings have led to the investigation of the relationship between breast cancer and autoimmune thyroid diseases (AITDs). The precise significance of this association remains elusive, and some reports have shown that the presence of thyroid peroxidase (TPO) antibodies is associated with a significant improvement in outcome among Breast cancer patients and is of similar importance to other prognostic indices such as axillary nodal status and tumour size .The aim of the present prospective study was to determine the prevalence of thyroid diseases in patients with breast cancer as compared with that in the general female population.

T3 EFFECT HYPERANDROGENISM IN WOMAN [12, 13]

The imbalance of thyroid hormones can cause the dysfunction of the reproductive system. The aim of our study is to evaluate

the thyroid hormone triiodthyronine's (T3) influence on women's hyper androgenism.

AUTOIMMUNE THYROID DISEASE

The common model of the onset of autoimmune thyroid disease involves an underlying genetic predisposition and a trigger(s) that initiate the cascade of events and sustain the process, culminating in thyroid hypofunction or hyper function. This process has been extensively studied and described. That 70%–80% of susceptibility to autoimmune thyroid disease is on a genetic basis. The specific genes involved include human leukocyte antigen-DR3, cytotoxic T lymphocyte-associated factor 4, CD40, protein tyrosine phosphotasegene, thymoglobulin (Tg), and TSH receptor [14].

THYROIDISM IN PREGNENCY

HYPOTHYROIDISM DURING PREGNANCY

Untreated overt hypothyroidism during pregnancy may increase the incidence of maternal hypertension, preeclampsia, anemia, postpartum haemorrhage, cardiac ventricular dysfunction, spontaneous abortion, fetal death or stillbirth, low birth weight, and, possibly, abnormal brain development . Evidence from a population based study suggests that even mild, asymptomatic, untreated maternal hypothyroidism during pregnancy may have an adverse effect on cognitive function of the offspring and that this outcome can be prevented by thyroid hormone replacement therapy. Mildly increased serum TSH levels during pregnancy might also increase the risk of fetal death, but whether treatment prevents this complication is not yet known. In most of these women, thyroid antibodies develop a finding that seems to be a risk factor for spontaneous abortion independent of thyroid hormone and TSH levels [15].

HYPERTHYROIDISM DURING PREGNANCY

Hyperthyroidism during pregnancy presents special concerns and is best managed collaboratively by an obstetrician and a clinical endocrinologist. Use of radioactive iodine is contraindicated during pregnancy because it crosses the placenta. Antithyroid drugs are the treatment of choice for hyperthyroidism during pregnancy, and propylthiouracil is clearly preferred over methimazole. Antithyroid drugs also cross the placenta, and

overtreatment with them may adversely affect the fetus. Therefore, the lowest possible dose of antithyroid drug should be used to maintain the mother's thyroid function at the upper limit of normal. Because pregnancy itself has an ameliorative effect on Graves' disease, the dose of Antithyroid drug required usually decreases as the pregnancy progresses. Often the Antithyroid drug can be discontinued before delivery. If surgical treatment does become necessary, it is best done during the second trimester of pregnancy. The patient's active participation in treatment is critical to the successful outcome of pregnancy in the presence of Graves' disease. Of importance, the patient must understand the risk of the disease, the pathophysiologic factors, and the mechanisms involved in therapy. Patient education will enhance adherence to recommended therapy as well as awareness of changes that may necessitate treatment alterations. With this background, the patient should become more aware of the problems that might occur and should alert her endocrinologist. The patient should also be informed about changes that may occur in her health or her

baby's health during the postpartum period [16]. She should be advised to inform the pediatrician of her thyroid disease and of the possibility that neonatal hyperthyroidism or hypothyroidism might develop in the baby. The infant's thyroid function must be tested at birth. The patient should also be aware that postpartum recurrence of the hyperthyroidism is likely. This finding can be related to the Graves' disease or postpartum thyroiditis. If overt hyperthyroidism due to grave's disease develops after delivery, the patient may be offered the alternative of resuming anti thyroid drug therapy or receiving radioactive iodine. Radioactive iodine therapy is contraindicated if the patient is breast-feeding or, of course, is pregnant again. Postpartum follow-up with appropriate assessment by a clinical endocrinologist should be continued until the patient is in a stable euthyroid state. Euthyroid pregnant patients treated for Graves' disease before the pregnancy may still have stimulating thyroid auto antibodies in the circulation, which can cross the placenta. Measurement of maternal TSI (TRAb) may be useful for

assessment of potential fetal risk; on the basis of clinical judgment, the endocrinologist can have this study done [17].

RELATION BETWEEN THYROIDISM AND BREAST CANCER

Ultrasonographic evaluation of the thyroid gland was conducted by the same radiologist using an ultrasound scan fitted with a hand-held 6.6–11 MHz linear transducer. The volume of each lobe was calculated using the following formula: volume = length × width × height × 0.479. Upper and lower normal lobe volume limits were 18 ml and 10 ml, respectively. Third, serum free Triiodothyronine (T_3) and free thyroxine (T_4) levels were determined, based on a solid-phase I radioimmunoassay designed for the quantitative measurement of free T 3 and free T levels in serum using Coat-ACount kit containing radioactive I $_{125}$ -T 3 or –T4 analogue Also, serum thyroid-stimulating hormone (TSH) levels were measured using a immunoradiometric assay designed for quantitative measurement of TSH in serum using Coat-A-Count kit containing radioactive I -polyclonal anti-TSH (Diagnostics Products Corporation, Los Angeles, CA, USA). The normal ranges were 2.2–6.8 pmol/l (1.4–4.4 pg/ml) for free T 3 I ^{125} , 0.8–2.0 ng/dl for free T 4 and 0.3–5.0 µIU/ml for TSH. Fourth, all patients underwent serological determination of thyroid autoantibodies based on a direct Anti-TPO radioimmunoassay kit for quantitative determination of anti-TPO autoantibodies. Also, autoantibodies specific for thymoglobulin were measured using a quantitative indirect enzyme immunoassay based on the sandwich method. The normal ranges were 0–60 IU/ml for antithyroglobulin antibodies and 0–20 IU/ml for anti-TPO antibodies. Finally, after informed consent had been obtained from each patient, fine-needle aspiration (FNA) of the thyroid gland was performed in breast cancer patients who had a palpable thyroid nodule. The aspiration was performed using a 22 guage needle and the smears were air dried and dyed with May–Gruenwald–Giemsa dye. FNA smears were considered diagnostic for autoimmune thyroiditis if there was an abundance of lymphocytes and plasmacytes in a diffuse pattern and/or coexistence of many lymphocytes and oxyphilic epithelial cells. Patients were separated into three groups

according to clinical and ultrasound findings: normal gland, diffuse goitre and nodular goitre. Those women without any breast or thyroid disease were the control group. Patients were also classified into the following subgroups according to menopausal and oestrogen receptor (ER) status: premenopausal and postmenopausal; and ER negative and ER positive [16].

FINE NEEDLE ASPIRATION

The use of fine needle aspiration (FNA) in the evaluation of a thyroid nodule is a relatively non invasive technique that can often be diagnostic and may prevent unwarranted surgery. The method of preparation used can give varying cytological appearances and each has advantages and disadvantages. Recently, newer techniques have been developed for example liquid based cytology, which allow lysis of blood and the preparation of further samples or a cell block for immunocytochemistry. However, the cytological appearances with liquid based cytology are somewhat different to those on conventional smears and further experience of the technique is required.

Indeed, one recent study has suggested that liquid based thin layer methods are not ideal for use in thyroid aspirates [17].
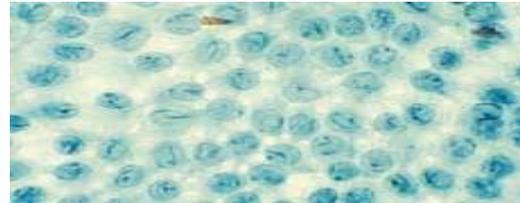

Figure 1: Fine needle aspirate of a papillary carcinoma showing nuclear grooves and optical clarity (Papanicolaou stain).

FOLLICULAR VARIANT OF PAPILLARY THYROID CARCINOMA PTC is the most common malignant tumor of the thyroid; its pathologic diagnosis is dependent solely on demonstration of typical nuclear cytology.FVPTC is the most common subtype of PTC, after excluding classic or usual variants of PTC. By light microscopy, FVPTC consists of follicles (either microfollicles or macrofollicles or mixtures of both) lined by cells with nuclear features of PTC. Some tumors are completely encapsulated, while there may show partial to total absence of a capsule.
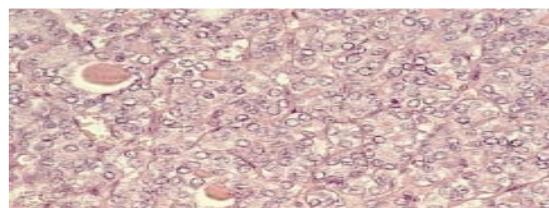
Figure 2: Follicular variant of papillary carcinoma (haematoxylin and eosin stain).
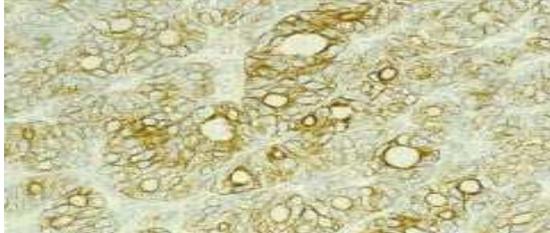

Figure3: Immunohistochemistry for cytokeratin in the follicular variant of papillary carcinoma.

According to these authors, this borderline or intermediate diagnosis will help to prevent unnecessary surgery and additional therapy, ie, radioactive iodine ablation.

DIAGNOSIS

A comprehensive history should be elicited, and a thorough physical examination should be performed including the following:

• Weight and blood pressure

• Pulse rate and cardiac rhythm

• Thyroid palpation and auscultation (to determine thyroid size, nodularity, and vascularity)

• Neuromuscular examination

• Eye examination (to detect evidence of exophthalmos or ophthalmopathy)

• Dermatologic examination

• Cardiovascular examination

• Lymphatic examination (nodes and spleen)

LABORATORY EVALUATION

The sensitive TSH assay is the single best screening test for Hyperthyroidism, and in most outpatient clinical situations, the serum TSH is the most sensitive test for detecting mild (subclinical) thyroid hormone excess or deficiency. Other laboratory and isotope tests may include the following:

• T_4 or free T_4

• Triiodothyronine (T4) radioimmunoassay (RIA) or free T3 abnormal results of T_4 or T measurements are often due to binding protein abnormalities rather than abnormal thyroid function. Therefore, total T 3 4 or T must be determined in conjunction with some measure of their thyroid hormone binding such as T resin uptake or assay of thyroid-binding globulin to yield a "free thyroid

hormone estimate." Commercial laboratories often call these methods free T 4 or free T3 even though they do not measure free hormone directly.

• Thyroid autoantibodies, including TSH receptor antibodies (TRAb) or thyroid-stimulating immunoglobulins (TSI) These studies are not routinely necessary but may be helpful in elected cases, such as in patients with hyperthyroidism during pregnancy.

• Radioactive iodine uptake

• Thyroid scan with either[123] I (preferably) or Tc pertechnetate. Such a scan is not a thyroid function test but is done to help determine the cause of the hyperthyroidism. The scan may also be useful in assessing the functional status of any palpable thyroid irregularities or nodules associated with a toxic goiter .Reverse T testing is seldom, if ever, helpful in clinical practice.

TREATMENT AND MANEGMENT

Three types of therapy are available for Graves' disease:
(1) surgical intervention,

(2) antithyroid drugs, and

(3) Radioactive iodine.

(1)SURGICAL INTERVENTION

Some physicians prefer surgical treatment of pediatric patients with Graves' disease or patients with very large or nodular goiters. Potential complications associated with surgical management of Graves' disease include hyperparathyroidism and vocal cord paralysis in a small proportion of patients. Surgeons trained and experienced in thyroid surgical procedures should perform this operation.

(2)ANTITHYROID DRUGS

 Antithyroid drugs, methimazole and propylthiouracil, have been used since the 1940s and are prescribed in an attempt to achieve a remission. The remission rates are variable, and relapses are frequent. The patients in whom remission is most likely to be achieved are those with mild hyperthyroidism and small goiters.

(3)RADIOACTIVE IODINE

 Radioactive iodine therapy is safe, but most treated patients become hypothyroid and require lifelong thyroid replacement

therapy. Some clinical endocrinologists are hesitant to use radioactive iodine to treat patients of childbearing age, but no evidence has suggested that such therapy has any adverse effects. Specifically, studies have found no effect on fertility, no increased incidence of congenital malformations, and no increased risk of cancer in patients treated with radioactive iodine or in their offspring. After administration of a dose of radioactive iodine, thyroid replacement therapy should be carefully initiated during the time the patient's thyroid function passes through the normal range into the hypothyroid range. The final thyroid replacement dose must be individualized. This approach promptly resolves the hyperthyroidism with a minimum of hypothyroid morbidity [16].

MECHANISM OF ACTION

Both T3 and T4 in their free form, diffuse across the cell membrane and bind to intracellular thyroid receptor in target tissues .they act by a mechanism rather similar to that of corticoids. After they enter the cell, T4 is converted to T3 and consequently T4 can be regarded as prohormone for T3. The later has greater

affinity than T4 for the thyroid receptor. When T3 is bound, the receptors change conformation, the corepressor complex is suppressed while a co-activator complex is recruited.This stimulates transcription, resulting in synthesis of proteins that produce many of actions of T3.

CHRONIC THYROIDITIS AND CLINICAL HYPOTHYROIDISM The treatment and management of chronic thyroiditis and clinical hypothyroidism must be tailored to the individual patient. Many clinical endocrinologists treat the goiter of chronic thyroiditis with levothyroxine, even in patients with a normal level of TSH, and all physicians will treat clinical hypothyroidism with levothyroxine replacement therapy. Furthermore,various brands of levothyroxine are not compared against levothyroxine standard. The patient should receive the same brand of levothyroxine throughout treatment. In general, desiccated thyroid hormone, combinations of thyroid hormones, or triiodothyronine should not be used as replacement therapy. The mean replacement dosage of levothyroxine is 1.6 g/kg of body weight per day, although the appropriate dosage may vary among

patients. The appropriate pace of treatment depends on the duration and severity of the hypothyroidism and on the presence of 4 other associated medical disorders.

The initial levothyroxine dosage may range from 12.5 ☐g daily to a full replace the dose based on the age, weight, and cardiac status of the patient and the severity and duration of the hypothyroidism. Importantly, patients should undergo reassessment and therapy should be titrated after an interval of at least 6 weeks following any change in levothyroxine brand or dose. The serum TSH level is most important, and a free T estimate may be included in the assessment as well. Once the TSH level is in the normal range, the frequency of visits can be decreased. The patient in the levothyroxine treatment by explaining the thyroid disease and potential consequences should result in improved adherence to recommendations. Thyroid hormone absorption can be affected by malabsorptive states and patient age. In addition, commercially available levothyroxine products may not be bioequivalent. Because levothyroxine has a arrow therapeutic range, small differences in absorption can result in subclinical or clinical hypothyroidism or hyperthyroidism. Drug interactions also present a problem. Certain drugs such as cholestyramine, ferrous sulphate, sucralfate, calcium and some antacids containing aluminium hydroxide interfere with levothyroxine absorption. Other drugs such as anticonvulsants affect thyroid hormone binding, whereas others such as rifampin and sertraline hydrochloride may accelerate levothyroxine metabolism and necessitate A higher replacement dose. The physician must make the appropriate adjustments in levothyroxine dosage in the face of absorption variability and drug interactions. Inappropriate levothyroxine replacement can result in increased costs because of the need for additional patient visits and laboratory tests [17].

PATIENT CARE IN THYROID DISORDER

Once the diagnosis of Grave's disease with hyperthyroidism has been established, the patient should be given a complete explanation of the illness and options for treatment. The goal is to involve the patient as a partner in the medical decision-making process and care, rather than Have the endocrinologist dictate the choice of

therapy. Patients who elect to receive, radioactive iodine should be given an explanation of the treatment, and a consent form for such therapy should be signed. After receiving radioactive iodine, patients should be given an instruction sheet that itemizes appropriate precautions and explains follow-up Management .The radioactive iodine uptake should be assessed before treatment to ensure adequate uptake at the time of therapy, to rule out the presence of a variant of thyroiditis or iodine contamination, and to help determine the dose of radioactive iodine.A thyroid scan is also useful in distinguishing toxic nodular goiter and toxic adenoma from Graves' disease. Typically, toxic nodular goiter is more resistant to radioactive iodine and frequently necessitates use of a larger dose. ß-Adrenergic antagonists provide symptomatic relief and can be administered before radioactive iodine is given. Because patients with hyperthyroidism may be relatively resistant to the effects of ß-adrenergic blocking agents, larger and more frequent doses may be necessary. The dose of these drugs can be tapered and discontinued once the patient no longer has

hyperthyroidism. In addition, in severe thyrotoxic states, adjuvant treatment can include organic or inorganic iodides and anti thyroid drugs after radioactive iodine therapy. After treatment with radioactive iodine, patients should have follow-up examinations at frequent intervals (varying from 4 to 6 weeks, but individualized for each case) until they are euthyroid and their condition is stable. Most patients will require full thyroid hormone replacement therapy. Patients usually become hypothyroid within 3 months and could begin receiving partial replacement doses of levothyroxine approximately 2 months after receiving radioactive iodine. This schedule is determined by laboratory testing and clinical evaluation. At this time, the patient's thyroid status is quickly changing from euthyroid to hypothyroid, and the TSH level may not be a good indicator of function because it fails to increase quickly. From 2 weeks to several months may elapse before TSH responsiveness is recovered, and free thyroid hormone estimate tests are more accurate than TSH values during this interval. When the condition of patients has stabilized, the frequency of visits and re-

evaluations can be extended. A common schedule for follow-up consultations is at 3 months, at 6 months, and then annually, but this can be modified on the basis of the physician's judgment [18].

CONCLUSION

The pathology of the thyroid gland presents the pathologist with a particular set of diagnostic problems. If best practice and the minimum data set guidelines are adhered to, the correct diagnosis should be reached in most cases. Newer techniques such as immunocytochemistry can certainly be helpful in more difficult cases but, as in all areas of pathology, histological features take precedence and good communication with the relevant clinical colleagues is paramount.

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